Oxidation of Alkenes with Use of Phase Transfer Catalysis¹

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ABSTRACT AND SUMMARY

The use of phase transfer catalysis (PTC) as an aid in the oxidation of long chain olefins with aqueous potassium permanganate (KMnO₄) in neutral and alkaline media and with aqueous ruthenium tetroxide (RuO₄) is reported. The phase transfer catalysts (PTCT) were either quaternary ammonium halides or crown ethers. The long chain olefins studied were 1-pentadecene, 9-octadecene, and methyl oleate. PTC not only increases the rate of these reactions but also gives good yields of reaction products. For example, cis-9-octadecene in methylene chloride reacted with aqueous KMnO₄ to give either dihydroxyoctadecane (80%) or pelargonic acid (80%), depending upon pH, when tetrabutylammonium bromide was used as the PTCT. When RuO₄ in conjunction with a PTCT was used as the oxidant, a quantitative yield of myristic acid was obtained from 1-pentadecene. The RuO4 oxidant was conveniently regenerated in situ from RuO₂ and sodium hypochlorite. This regeneration is facilitated with a PTCT.

INTRODUCTION

Recent years have witnessed the ascendence of a new technique in organic chemistry in which reactions conducted in an aqueous-organic two phase system are improved by the presence of an ammonium or phosphonium salt or a crown ether (1-3). The general term applied to this method of facilitating two-phase reactions, which normally proceed either slowly or not at all, is phase transfer catalysis (PTC). PTC promotes these heterogeneous reactions by transferring the water soluble reactant into the organic phase where reaction with the organic soluble substrate occurs. Reactions improved by the application of PTC include: the generation of dichlorocarbene (4), the alkylation of carbonyl and related compounds (5), nucleophilic substitution reactions (6), and the oxidation of alkenes by aqueous potassium permanganate (7-10). The latter studies found that α -olefins are quantitatively oxidized by neutral aqueous potassium permanganate to carboxylic acids containing one less carbon atom than the starting olefin had, when the reactions are carried out with either a crown ether (7) or quaternary ammonium salt (8,10). With cycloalkenes, such as cyclohexene, diacids were obtained in high yields (8). The hydroxylation of cyclic olefins to cis-diols with basic potassium permanganate and quaternary ammonium phase transfer catalysts (PTCT) has also been investigated (9).

In view of the experimental difficulties encountered in the non-phase transfer catalyzed oxidation of water-insoluble internal olefins with aqueous potassium permanganate (11,12), we undertook the present investigation to determine if these reactions could be facilitated by PTC. We also studied the oxidative cleavage of olefins to carboxylic acids with ruthenium tetroxide with the aid of PTC. Ruthenium tetroxide is conveniently generated in situ from ruthenium dioxide by action of an oxygen donor, such as sodium metaperiodate or sodium hypochlorite (13); these oxidants also regenerate RuO₄ from any RuO₂ produced during the

oxidation. This regeneration or spent oxidant is facilitated by PTC.

EXPERIMENTAL PROCEDURES

Materials

cis-9-Octadecene was prepared by the lithium aliminum hydride reduction of the tosylate of oleyl alcohol (14). Purity as determined by gas liquid chromatography (GLC) and thin layer chromatography (TLC) was 98%. 1-Pentadecene (99%), methyl oleate (98%), tetrabutylammonium bromide, cetyltrimethylammonium bromide and dicyclohexyl-18-crown-62 were obtained from Eastman Chemical Company (Rochester, NY). Ruthenium dioxide² (45%) was obtained from Engelhard Industires. Sodium hypochlorite solution (5.75%), Chlorox, was purchased at a local supermarket.

Oxidations with Potassium Permanganate

Neutral potassium permanganate: A solution of KMnO₄ (30 mmole) in H₂O (50 ml) was placed into a 250 ml Morton flask equipped with a magnetic stirrer, addition funnel, and condenser. A solution of tetrabutylammonium bromide (3 mmole) in CH₂Cl₂ (30 ml) was added to the flask, and the two phases were vigorously stirred for 1 hr at 5-10 C. 9-Octadecene, 1a, (10 mmole) was added dropwise to the stirred reaction mixture over a 15 min period at 10 C. The mixture was then stirred for 12 hr at room temperature. The precipitated MnO₂ was reduced by bubbling SO₂ through the reaction mixture, and the mixture was acidified to pH 2 by the addition of conc. HCl. The CH₂Cl₂ layer was separated from the aqueous layer, and the latter was extracted with CH₂Cl₂ (2 x 25 ml). The combined organic layers were washed with H₂O (3 x 25 ml), dried over MgSO₄ and the solvent removed in vacuo. The crude oxidation product, after esterfication with BF₃·MeOH reagent, was analyzed by GLC (Table I). Products were identified by comparison with authentic samples by both GLC and TLC.

The bulk of methyl pelargonate, 2a, was then removed by distillation. Upon cooling,the yellow pot residue solidified. Recrystallization from petroleum ether gave yellow crystals of 9,10-diketooctadecane, 3, mp 54.4-55 C; IR: 1710 cm⁻¹; mass spectrum: m/e, 282 (M⁺), 141 (100%). From the filtrate, pure 9-keto-10-hydroxy-octadecane, 4, was isolated by preparative TLC on silica gel (benzene-Et₂O-MeOH, 95:5:1); IR: 3400 and 1710 cm⁻¹, mass spectrum: m/e, 284 (M⁺).

Basic potassium permanganate: Into a 250 ml Morton flask equipped with a magnetic stirrer, addition funnel, and condenser was placed a solution of 9-octadecene (10 mmole), and tetrabutylammonium bromide (3 mmole) in CH₂Cl₂ (50 ml), and 50 ml of aqueous sodium hydroxide solution (40%). The stirred two phase reaction mixture was cooled to 0 C, and a solution of KMnO₄ in H₂O was added dropwise over a period of 1.5 hr. When addition was complete, the reaction mixture was allowed to warm and was stirred at room temperature for 12 hr. The precipitated MnO₂ was reduced by reaction with SO₂, the mixture was acidified with conc. HCl, and the organic layer was sepa-

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²Proper precautionary measures should be exercised when handling crown ethers and ruthenium tetroxide in view of their poisonous nature and strong oxidizing properties.

rated. The aqeuous layer was extracted with CH_2Cl_2 (3 x 50 ml) and the combined organic layers were washed with H_2O , dried over $MgSO_4$ and the solvent was removed in vacuo. The crude 9,10-dihydroxyoctadecane was purified by crystallization from ethanol, mp 128-130 C [lit (15) mp = 129-130 C]. Yield data are given in Table II.

RuO₄ Oxidation of 1-Pentadecene

A solution of 1-pentadecene, 1b, (13 mmole) and tetrabutylammonium bromide (12.4 mmole) in CH₂Cl₂ (50 ml) was placed into a 250 ml Morton Flask equipped with a mechanical stirrer, thermometer, and addition funnel. Solid RuO_2 or $RuCl_3$ (0.37 mmole) was then added to the stirred reaction mixture. Aqueous sodium hypochlorite (96 ml of 5.75% soln, 74 mmole) with added NaOH (70 mmole) was added to the stirred CH2Cl2 solution while the temperature was maintained between 17-22 C by means of an ice bath. The stirring was continued until the starch iodide test for active chlorine was negative, at which time the reaction mixture was acidified with conc. HCl. The organic layer was separated and the aqueous layer extracted with CH2Cl2 (3 x 50 ml). The combined organic extracts were washed with H₂O, dried with MgSO₄, and the solvent removed in vacuo to give crude myristic acid which, after esterification, was identified by comparison with an authentic sample by GLC.

Oxidation of cis-9-octadecene with RuO_2 -sodium hypochlorite was carried out in a similar manner with the exception that the latter reactions required longer reaction times. For yield data see Table III.

RESULTS AND DISCUSSION

As a model for the phase transfer catalyzed oxidation of internal olefins to carboxylic acids, we studied the oxidation of cis-9-octadecene, la, with aqueous potassium permanganate. This olefin was selected as a model for monounsaturated fatty esters because its symmetry facilitates the identification of its oxidation products. The initial experimental conditions used were similar to those previously used in the oxidation of terminal alkenes (7,10). The oxidation of la with aqueous KMnO₄ was initially studied with benzene as the solvent and cetyltrimethylammonium bromide (CTAB) as the PTCT (exp. 1, Table I). The molar ratio of KMnO₄ to cis-9-octadecene used in this and subsequent experiments was 3:1. This rato was selected to ensure an excess of oxidant over the stoichiometric amount (2.67). The concentration of the PTCT employed was arbitrarily set at 1/10 of the molar concentration of oxidant. Under the above conditions, the oxidation of 9-octadecene resulted in a 50% yield of the expected cleavage product pelargonic acid, 2a, as determined by GLC of the esterified reaction mixture. Aside from 2a and unreacted 1a (5%), GLC and TLC of the crude reaction product indicated the presence of two additional oxidation products (eq. I). The two byproducts were identified by spectroscopic and chemical data to be 9,10-diketooctadecane 3 (27%) and the α -ketol derivative 4 (5%), eq. I.

The formation of oxidation products similar to 3 and 4 has also been reported when alkenes are oxidized with KMnO₄ in the absence of a PTCT. It has been shown (11,12) that the best yields of ketol and diketo derivatives, such as 3 and 4, were obtained when the reaction was carried out in the pH range 6 to 7, whereas at pH 3 cleavage to

TABLE I

Oxidation of 9-Octadecene with KMnO₄

Exp. #	Solvent	Phase transfer catalyst ^a	% Yield C9 acidb,c	% Yield diold,e
1	C ₆ H ₆	СТАВ	50	_
2	CH ₂ Čl ₂	CTAB	70	_
3	CH ₂ Cl ₂	TBAB	80	_
4	CH ₂ Cl ₂	CE	80	_
5	CH ₂ Cl ₂	CTAB		30
6	CH ₂ Cl ₂	TBAB		64
7	CH_2CL_2	CE	<u> </u>	80
8	С ₆ Н ₆ -	CE	<u> </u>	10

^aPhase transfer catalyst: CTAB = cetyltrimethylammonium bromide, TBAB = tetrabutylammonium bromide, CE = dicyclohexyl-18-crown-6.

bMole ratio olefin-KMnO₄-catalyst = 10:30:3.

cYield data obtained from GLC of methyl ester.

d_{Mole} ratio alkene: KMnO₄: NaOH: catalyst = 10:30:30:3.

e Yields are based on isolated diol.

TABLE II

Oxidation of Alkenes by RuO4-NaOCl

Exp. # Alkene		Reactant ^a ratio	Time (hr)	Solvent	% Yield acidb
1	1bc	Α	6		33
2	1b	Α	6	CC14	10
3	1 b	В	6	CH ₂ Cl ₂	100
4	1 b	C	6	CH ₂ Cl ₂	100
5	1ad	C	6	CH ₂ Cl ₂	26
6	1a	С	12	CH ₂ Cl ₂	52
7	1a	C	18	CH_2CI_2	84

 a Mole ratio alkene-RuO₂-TBAB:NaOCl:NaOH = A = 1:6:0:14:5 B = 1:6:1:14:5 C = 1:0.03:1:14:5

bYields obtained by GLC of methyl ester.

cb = 1-pentadecene

 $d_{1a} = cis$ -9-octadecene

carboxylic acids is the major reaction. Lowering the pH of the aqueous KMnO₄ with sulfuric acid in the present study, however, did not increase the yields of cleavage product. Accordingly, from the above results we can conclude that the oxidation of olefins occurs in the organic phase, since the product distribution (eq. I) more closely resembles that obtained from neutral aqueous KMnO₄ oxidations. Moreover, if the same two-phase oxidation reactions are carried out in the absence of the PTCT, CTAB, 95% of unchanged olefin is recovered. Increasing reaction times to 20 hr or changing the mode of addition of reactants did not improve the yields of cleavage product 2a significantly. Improved yields of 2a, however, could be obtained (≅70%) by increasing either the amount of KMnO₄ (mole ratio of KMnO₄:1a of 4:1) or by increasing the amount of catalyst (mole ratio of CTAB:KMnO₄ of 1:1).

Other reports have shown that changes in reaction solvent and PTCT can markedly affect the course of phase transfer catalyzed reactions (16,17). We also studied changes in the above two variables to determine if the yields of 2a could be improved. A change of solvent from benzene to CH₂Cl₂ with CTAB catalyst (exp 2, Table I) increased the yield of 2a to 70% with a concomitant decrease in yields of byproducts 3 and 4. This result agrees with the general principle that chlorinated hydrocarbons are generally the best solvents for carrying out phase transfer catalyzed reactions. With CH2Cl2 as solvent and a change of PTCT from CTAB to tetrabutylammonium bromide (TBAB), the yield of 2a improved to 80% (exp. 3, Table I). When benzyltrimethylammonium bromide was used in place of CTAB, poorer yields of 2a were obtained and the amount of byproducts 3 and 4 increased. Similar variations in yields of oxidation cleavage products with changes in ammonium salt structure have been noted by Herriott (16). In general, Herriott found that an onium salt must have the proper hydrophobic-hydrophilic balance to be an efficient PTCT. This balance is generally found when the total number of carbon atoms about the nitrogen atom is in the range of $C_{16}-C_{20}$. Below this range the partition coefficient of the onium salt favors the aqueous phase, whereas much above this range (e.g., tetradecylammonium bromide) emulsification problems complicate the reaction procedure. An additional factor affecting PTCT activity is the structure of the onium salt catalyst. Symmetrical onium salts are generally more efficient PTCT than are unsymmetrical onium salts with approximately the same carbon number (compare TBAB with CTAB, exp. 2 and 3, Table I).

Another commonly used class of PTCT is the crown ethers (8,10). These catalysts, in contrast to the onium salts, are neutral macrocyclic ethers that transfer KMnO₄ into the organic phase by complexing potassium ion. When dicyclohexyl-18-crown-6 was substituted for TBAB and CH₂Cl₂ was used as solvent for the oxidation of cis-9-octadecene with KMnO₄, an 80% yield of pelargonic acid 2a was obtained (exp. 4, Table I). In contrast, with benzene as the solvent in the above reaction, the yield of 2a was similar to that obtained with CTAB in benzene. This again points out that CH₂Cl₂ is a better organic phase than benzene for conducting phase transfer catalyzed reactions. TBAB and the crown ether are comparable in facilitating the oxidation of 1a to 2a (exp. 3 and 4 in Table I). It would appear that the onium salts are the preferred catalysts for the phase transfer catalyzed oxidation of alkenes to carboxylic acids, because of higher cost of the crown ethers and their potential toxicological side effects.

To apply PTC to fatty esters, the oxidation of methyl oleate 6 with aqueous $KMnO_4$ was studied. The PTC system employed was CH_2Cl_2 solvent and TBAB catalyst, eq II. The crude oxidation product, after esterification, was analyzed by GLC. The latter showed the presence of the expected cleavage products methyl pelargonate 2a (67%) and monomethyl azelate 7 (72%). The crude product also showed evidence of other oxidation products, presumably the diketo and ketol derivatives, but these were not conclusively identified.

In addition to the oxidations carried out in neutral medium, we also investigated the phase transfer catalyzed oxidation of 1a with KMnO₄ in alkaline medium. KMnO₄ oxidation of 1a at higher pH favors cis-hydroxylation of 1a to its erythro dihydroxy isomer 5, eq. III. We obtained the best yields of 5 with dicyclohexyl-18-crown-6, in CH₂Cl₂ solvent as the phase transfer catalyst (exp. 7, Table I), eq. III. Of the onium salts studied, CTAB gave yield of 5 while TBAB gave intermediate yields of 5 (exp. 5 and 6, Table I). When we changed the solvent from CH₂Cl₂ to benzene, the crown ether gave a 10% yield of diol 5, the remainder being unreacted olefin. This result again points out the importance of solvent selection in performing phase transfer catalyzed reactions. The phase transfer catalyzed hydroxylation of cis-9-octadecene with basic KMnO₄ occurs because of the ability of the onium salts and the crown

ethers to transfer both hydroxide ion and permanganate ion into the organic phase. The transfer of hydroxide ion into the organic phase is important, since the mechanism of hydroxylation of alkenes with KMnO₄ has been shown to require hydroxide ion (18).

$$\begin{array}{c} \text{CH}_{3}(\text{CH}_{2})_{7} & \text{(CH}_{2})_{7}\text{CH}_{3} & \xrightarrow{\text{KMnO4,NaOH}} \\ & \text{C} = \text{C} \\ & \text{H} & \text{H} & \\ & & \\$$

Attempts to hydroxylate methyl oleate using the basic KMnO₄ procedure gave us poor yields (<25%) of the dihydroxy derivative. This result was probably due to the saponification of the ester which resulted in serious emulsion problems during the course of the reaction.

An alternative method for oxidizing alkenes uses ruthenium tetroxide as the oxidant. Ruthenium tetroxide (RuO₄) is a very powerful oxidizing agent which is soluble in a variety of hydrocarbon solvents (19). For example, a performed solution of RuO₄ in carbon tetrachloride rapidly oxidizes cyclohexene and 1-octene to adipaldehyde and heptaldehyde (20), respectively. More recently, it has been claimed that when alkenes are oxidized with RuO4 formed in situ from RuO2 and sodium hypochlorite and no organic solvent is used, carboxylic acids are the major product (21,22). We have not been able to reproduce the results obtained in the previous work (21). So, we reexamined this reaction by studying the oxidation of cis-9-octadecene, 1a, and 1-pentadecene, 1b, with ruthenium tetroxide generated in situ by the reaction of sodium hypochlorite with RuO2, eq. IV.

$$\begin{array}{ccc}
R & R' \\
C = C & RuO_2, NaOC1 \\
NaOH, TBAB & R-CO_2H
\end{array}$$
(IV)

Reaction of 1b with RuO2-sodium hypochlorite solution for 6 hr gave poor yields (<10%) of the expected myristic acid, 2b. Aside from recovered 1b other products formed in this reaction were identified as the dichloro- and chlorohydrin derivatives of 1b. The latter two addition products resulted from the reaction of 1b with chlorine and hypochlorous acid formed by the disproportionation of sodium hypochlorite. To suppress the formation of chlorinated byproducts, we repeated the experiment with added base, NaOH (exp. 1, Table II). We obtained a 33% yield of 2b and observed no chlorinated byproducts. In a second experiment when we used carbon tetrachloride as solvent for 1b, the yield of 2b decreased to 10% (exp. 2, Table II). Since we were unable to obtain good results using the reported procedures, we decided to see if PTC would facilitate this reaction.

In the above two-phase system, the oxidation of 1h by ruthenium tetroxide occurs in the organic phase. The ruthenium dioxide precipitate formed in this process then migrates to the interface where it is reconverted to

ruthenium tetroxide by the cooxidant which remains in the aqueous phase. Accordingly, vigorous mixing of the phase is required to obtain reasonable yields in short reaction times. Transferring hypochlorite anion into the organic phase should facilitate the rapid reoxidation of RuO2 to RuO4 and thus accelerate the rate of oxidation of 1b. We conducted reaction of 1b with RuO₂-sodium hypochlorite oxidant with the PTCT tetrabutylammonium bromide in CH₂Cl₂ solvent (exp. 3, Table II). This cleavage of 1b to 2b was quantitative within the same reaction time period as those of experiments in the absence of PTC (compare exp. 3 and 4, Table II), and vigorous mixing of the reactants was not required. More importantly, in the absence of the RuO2 oxidant, we recovered 1b intact. Additionally, we achieved quantitative conversions of 1b to 2b within the same reaction times as when we increased the molar ratio of 1b to RuO₂ from 1:6 to 32:1 (exp. 4, Table II). Higher molar ratios of 1b to RuO2 could be used but these reactions required longer reaction times. In those experiments in which we used RuO2 in catalytic amounts, the actual oxidant being consumed is sodium hypochlorite. The overall reaction of an alkene with the catalytic RuO2hypochlorite system requires a stoichiometry of 4 moles of NaOCl per mole of alkene. To ensure complete oxidation of the double bond, we employed the actual molar ratio of 6:1 NaOCl to alkene.

Application of the phase transfer catalyzed RuO_4 -NaOCl oxidation technique to 9,10-octadecene resulted in lower yields of pelargonic acid 2a, during the same reaction time used for 1-pentadecene (compare exp. 4 and 5, Table II). However, the conversion of 1a to 2a increased when we employed longer reaction times (exp. 5-7, Table II). An important aspect of this oxidation reaction is the complete absence of byproduct formation as compared to the KMnO4 oxidation procedure.

The oxidation of water-insoluble alkenes by KMnO₄ or RuO₄ has been facilitated by PTC and high yields of reaction products were obtained. The application of PTC to the above methods of oxidation offers several advantages over

conventional procedures. For example, the experimental procedures are relatively simple in that neither water-micible solvents nor the preparation of oil/water emulsions are required. Neither high dilution techniques nor control of pH are needed to ensure good yields. The reaction products are isolated easily.